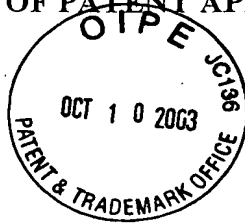


IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:
Howard Preissman
Serial No. 09/828,539

Filed: April 5, 2001

For: Enhanced Visibility Materials for
Implantation in Hard Tissue



Art Unit: 3738

Examiner: Miller, Cheryl L

Atty Docket No. PALX-002CON

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Brief of
Appeal
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Commissioner for Patents

BRIEF ON APPEAL

Sir:

This appeal is from the decision of the Patent Examiner dated March 11, 2003, finally rejecting claims 33-44 and 46-53.

A fee transmittal covering the \$165.00 Government fee and two extra copies of this brief, are being filed herewith.

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 50-0815. This paper is submitted in triplicate.

REAL PARTY IN INTEREST

The real party in interest in this appeal is Parallax Medical, Inc. per the assignment of the invention that has been made from Howard Preissman.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

STATUS OF CLAIMS

Claims 33-44 and 46-53 are pending in the present application. Claims 40-44 stand rejected under 35 U.S.C. §102(b) as anticipated by Ersek, *et al.* (USPN 5,258,028). Claims 33-39

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and 46 stand rejected under 35 U.S.C. §103(a) as unpatentable over Draenert, *et al.* (USPN 6,080,801) in view of Ersek. Claims 47-53 stand rejected under 35 U.S.C. §103(a) as unpatentable over Cooke *et al.* (USPN 5,336,699) in view of Ersek.

STATUS OF AMENDMENTS

All amendment to the claims have been entered. The claims, as amended, are presented in the **Appendix A** hereto.

SUMMARY OF THE INVENTION

The present invention relates to compositions for use as tissue implants, preferably hard tissue implants. More particularly, the present invention is directed to compositions which are more easily viewed by imaging techniques, during the implantation thereof, than compositions that are presently known and used. A particularly advantageous use of the present invention is for percutaneous injection of hard tissue implant materials, although the invention is not to be so limited. Page. 1, lines. 11-16. Exemplary embodiments of the invention are shown in Figures 2-4. See, **Appendix B**.

One aspect of the invention concerns an injectable composition comprising a biocompatible matrix, with radiopaque particles of a size range between about 120 μ and about 2200 μ mixed in the matrix, with the addition of liquid contrast agent.¹ See, page. 3, line. 16 – page. 4, line 24. The nature of the biocompatible matrix is optionally in the form of a slurry or of such a quality to form a hard tissue implant material. Regardless, the size of the particles may be selected to provide contrast (*i.e.*, be of a size in the 120 μ to 350 μ range) or be larger in size to perform a “tracer” function. By performing the latter function, what is meant that the particles will be clear and individually identifiable under fluoroscopy so that

¹ (Claim 33) An injectable composition comprising:
a biocompatible matrix;
radiopaque particles mixed within said biocompatible matrix, said radiopaque particles having a particle size between about 120 μ and 2200 μ ; and
liquid contrast agent.

that the motion of implant material may be observed. Such activity is described at page 7, line 25 – page 8, line 11 in reference to Figure 2.

Another aspect of the invention represented in the claims on Appeal is for an injectable composition comprising a flowable matrix, with radiopaque particles in the flowable matrix, where the radiopaque particles have a size between about 350 μ and about 2200 μ so as to be individually visible during implantation, with the addition of another set of radiopaque particles for contrast having a particle size up to about 350 μ .² Yet another aspect of the invention represented in the claims on Appeal is for an injectable composition comprising a hard tissue implant biocompatible matrix, with and radiopaque particles mixed in the biocompatible matrix, where radiopaque particles having a particle size between about 120 μ and about 2200 μ .³ Unlike the first invention summarized above, the second and third do not require the inclusion of liquid contrast agent. Yet, the second one requires the selection of particles from two different size ranges. Particles in the smaller range provide contrast, while those in the larger perform the “tracer” function described above. The third invention embraced by the noted claims simply requires that the implant material matrix be of a certain kind.

Namely, it is necessarily a “hard tissue” implant material matrix. By a “hard tissue” implant material, what is meant is material or a compound that is suited for use in effecting vertebroplasty or augmenting other bone-type sites. The hard tissue implant material preferably includes Polymethylmethacrylate (PMMA). Alternative hard tissue implant materials that may be used in the variation of the invention covered by claim 47 include

² (Claim 40) An injectable composition comprising:

a flowable matrix;

radiopaque particles in said flowable matrix, said radiopaque particles having a size between about 350 μ and about 2200 μ so as to be individually visible during implantation, and radiopaque particles for contrast having a particle size up to about 350 μ .

³ (Claim 47) An injectable composition comprising:

a hard tissue implant biocompatible matrix; and

radiopaque particles mixed within said biocompatible matrix, said radiopaque particles having a particle size between about 120 μ and 2200 μ .

hydroxyapatite, various formulations of biocompatible calcium phosphates, biocompatible calcium sulfates, demineralized and/or mineralized bone particles, polymer based implants including polyglycolic acid and or polylactic acid compounds, collagen and/or collagen derivative preparations alone or in combination with other biomaterials, chitin and/or chitosan preparations, bioglasses including oxides of silicon, sodium, calcium and phosphorous and combinations thereof, and other known materials which are acceptable for use as hard tissue implant materials including osteogenic and osteoinductive compositions, and combinations thereof. Page 3, line 25 – page 4, line 9. Materials which do not offer a measure of structure/rigidity when cured do not qualify within this class of materials as understood by those with skill in the art.

In any case, all of the noted variations of the invention are optionally used in performing vertebroplasty. The general procedure for performing percutaneous vertebroplasty includes the percutaneous injection of PMMA or other bone implant material into the damaged or fractured bone tissue of a vertebra. During injection of the bone implant material, fluoroscopic imaging or another imaging technique is used to track the path that the bone implant material takes as well as its final position upon implantation. It has been known to use contrast agents such as barium sulfate powder mixed in with the hard tissue implant material to aid in the visibility of the material under medical imaging. However, the barium sulfate powders and other contrast agents used prior to Appellant's invention were generally very fine. This type of contrast agent is fairly effective once a given mass of the mixture of it with the bone implant material has accumulated at an implant site. However, for purposes of tracking the flow and leading edge surfaces of a bone implant material during injection, or for viewing small volumes of the implant material, such use of contrast agents were inadequate. This inadequacy would become especially important during injection of liquid or flowable bone implant materials, as is the case with percutaneous vertebroplasty, since viewing of the path taken by the implant material is very important. That is because the bone implant material may take a path where it begins to enter the venous system and/or extravasate into and

around neural structures, where it is not only unwanted, but where it could have severely damaging effects. Thus, an improvement in the visibility of implant materials – especially bone implant material - during injection was needed. Page 2, lines 4-23.

The noted aspects of the invention are employed to meet this need. The invention of claim 33, offers a dual-mode of contrast to achieve the ends of providing a safer and, thus, more effective injectable implant material. Particularly, it provides for liquid contrast agent and particles of a size range of about 120μ to 2200μ in the implant material matrix. In this regard, the Specification notes that particles in the size range of 350μ to 2200μ are usually clearly and individually visible under standard medical imaging. But at higher magnifications (as contemplated in the Specification that may be used, *e.g.*, at page 7, line 12), the smaller particles may be as well. Thus, in such instances, the smaller particles (as small as 120μ) used in connection with liquid contrast agent can serve the “tracer” purpose in the composition. At standard (4X fluoroscopy) however, the addition of liquid contrast agent to a composition with smaller particles, will simply provide greater contrast, without the noted deleterious effects of providing a composition too heavily loaded with particulates. Where the liquid contrast agent is used with larger particles (those offering a tracer function under 4X fluoroscopy), the operation of the invention is basically as where smaller particles are used for contrast instead.

Like claim 33, claim 40 is directed toward an sort of injectable composition. However, claim 40 calls for the addition of radiopaque particles in each of a larger and smaller size range. The purpose is to each (respectively) offer tracer and contrast features of the invention in any form of flowable implant material.

Unlike independent claims 33 and 40, claim 47 (and those dependent therefrom) is(are) specifically directed to a hard tissue implant material composition. The radiopaque particles to be included in the (still) injectable composition are between about 120 and 2200μ .

Of course, the functional properties of such particles in the context of the invention are addressed above.

ISSUES ON APPEAL

I. WHETHER THE TEACHINGS OF ERSEK SUPPORT ANTICIPATION OF CLAIMS 40-44

The Examiner has asserted that Ersek *et al.* (Ersek) discloses a flowable matrix and radiopaque particles having a size range between 350 μ and 2200 μ , 570 μ and 220 μ , 450 μ and 1600 μ or 570 μ and 1150 μ , and further having smaller particles having a size between 120 μ and 350 μ . As of the Amendment filed December 19, 2002 Appellant has asserted that the reference does not even teach the use of two different particle size ranges.

II. WHETHER A PRIMA FACIE CASE OF OBVIOUSNESS HAS BEEN ESTABLISHED FOR THE INJECTABLE COMPOSITION OF CLAIMS 33-39 AND 46 OVER DRAENERT IN VIEW OF ERSEK

The Examiner asserted that "Ersek teaches radiopaque particles having an increased size of 120 μ to 2200 μ , in order to optimize the size for aiding in injection, and avoiding the adverse effects of smaller particles." Appellant contends that the former expressed motivation (optimizing for injection) is not a motivation taught by Ersek, and further that the latter expressed motivation (avoiding adverse effects of smaller particles) is not a motivation applicable to justifying Draenert in view of Ersek. In any case, it is asserted that Draenert and Ersek are not properly combined as references for either reason of being non-analogous or for reason of the teachings of Ersek changing the principle of operation of Draenert. Finally, it is asserted that the proposed combination of Draenert and Ersek fails to meet certain limitations of claims dependent from claim 33.

III. WHETHER A PRIMA FACIE CASE OF OBVIOUSNESS HAS BEEN ESTABLISHED BY VIRTUE OF PROPER COMBINATION OF ERSEK AND COOKE, OR – IF SO – WHETHER THE COMBINED TEACHINGS MEET THE LIMITATIONS OF CLAIMS 47-53

Again, as asserted in Appellant's Amendment dated December 19, 2002, it was put forth that Cooke, *et al.* (Cooke) and Draenert represent non-analogous art, rendering their combination impermissible. Further, in view of the teaching of each reference, it was

asserted that the motivation of the combination was inadequate – or inapplicable. Finally, with respect to claims 52 and 53, the above-referenced failure of Ersek to disclose the use of two different size ranges of particles was noted as reason for withdrawal of the rejection.

GROUPING OF CLAIMS

Claims 33-34 and 36 stand together; 37-39 and 46 stand together; claim 35 stands alone. Arguments applicable to claims 33-34 and 36 offer further reasons for allowance of claims 35, 37-39 and 46.

Claims 40-44 stand together.

Claims 47-51 stand together; claims 52 and 53 stand together, though arguments applicable to claims 47-51 offer further reasons for allowance of claims 52 and 53.

ARGUMENTS

I. WHETHER THE TEACHINGS OF ERSEK SUPPORT ANTICIPATION OF CLAIMS 40-44

The Office Action dated March, 11, 2003 rejected claims 40-44 under 25 U.S.C.

§102(b) as anticipated by Ersek. It was asserted that:

Ersek discloses a flowable matrix (31) and radiopaque particles (30), (col. 3, lines 7-8, 15-18; col. 10, lines 23-26) having a size between 350 μ and 2200 μ , 570 μ and 2200 μ , 450 μ and 1600 μ , or 570 μ and 1150 μ (col.5, lines 43-45), and further having smaller particles having a size between 120 μ and 350 μ (col.5, line 64-col.6, line 2).

Further, in the section of the Office Action titled “Response to Arguments”, it was stated that:

Applicant’s arguments filed December 27, 2002 have been fully considered by they are not persuasive. In response to applicant’s argument to the Ersek reference, Ersek does indeed disclose tow different particle sizes within one composition, including smaller and larger particles within the ranges claimed (see col.3, lines 45-47; col.5, lines 64-68; col. 6 lines 1-2) ...

If it were not for the fact that the Examiner has provided specific citations to the reference,

Appellant would wonder whether discussion was even focused on the same reference.

The reason for such curiosity would stem from the fact that that Ersek very clearly fails to disclose a composition containing particles in two size ranges (much less those claimed). To prove this, Applicant references the text cited by the Examiner. Specifically, col.3, lines 45-47 states:

While in most situations the particles are of a random size and configuration, but within the constraints of the size indicated, it is generally desirable that the particles be of a generally uniform configuration whenever possible.

Col.5, lines 64-68 and col. 6 lines 1-2 states:

Further, with respect to particle size, it will be appreciated that particle size, particularly of those species contained in preparations utilized in prior injectable compositions tend to vary over a range within any group of particles so that there will be a percentage of the group and a percentage of the group smaller than at a target size in any such composition.

With respect to these passages, they merely talk about expected, random variation in particle size. Nowhere in these passages cited by the Examiner is the notion of providing two discrete sets of different sized particles in a composition, where each set has an acceptable size range.

All Ersek teaches is that sometimes the composition it describes will have some percentage of larger or smaller particles. Thus, it merely teaches the concept of random variation about an “optimal particle size” as it expresses at col. 6: line 9.

Appellant’s invention involves anything but the random. The claims require selection of particles within two discrete particle size ranges. Nothing else will do in this regard.

In Ersek, the reference merely teaches using microparticles anywhere in a size range “generally between 30 and 3000 microns” or in a tighter range. (Claim 1, etc.) Some variation is expected within the range, but no subsets are carved out of the range. No selection of different size ranges is presented in or fairly suggested by the reference. That is to say, the reference does not teach using some of the smaller particles with some of the larger. Ersek has nothing to do with such an approach.

II. WHETHER A PRIMA FACIE CASE OF OBVIOUSNESS HAS BEEN ESTABLISHED FOR THE INJECTABLE COMPOSITION OF CLAIMS 33-39 AND 46 OVER DRAENERT IN VIEW OF ERSEK

Claims 33-39 and 46

Claims 33-39 and 46 were rejected under 35 U.S.C. §103(a) as being unpatentable over Draenert in view of Ersek. In discussing Ersek, the Examiner asserted that, “Ersek teaches radiopaque particles having an increased size of 120 μ to 2200 μ , in order to optimize the size for aiding in injection, and avoiding the adverse effects of smaller particles.”

While the latter characterization of the teaching in Ersek is not disputed, the first assertion (that the reference teaches providing smaller and larger particles to ease injection) is disputed – in the strongest terms. Appellant is aware of no such teaching in the reference. As before (see, note 1 in the Amendment dated December 19, 2003) it is requested that the Examiner point out such teaching in the reference. If not, Appellant contends, as asserted before, that such a basis is not appropriate to premise a rejection upon.

As for Ersek’s teaching the use of larger particles to avoid the adverse effects of smaller particles - such teaching are not applicable in the context of the Draenert reference, which teaches improvements in the field of hard tissue implant materials. To review Ersek, it teaches using particles of a larger size to avoid problems observed with respect to macrophage engulfment of particles of a size less than 60 μ and sub-micron particle transport within the body.

Where the carrier material is of the sort employed by Ersek, such concerns are certainly valid in which the vehicle (carrier) employed for delivering the filler particles is a hydrogel or collagen that will itself dissipate or be absorbed by the body, leaving the particles unsecured. In marked contrast, Draenert deals with a hard tissue implant material – *e.g.*, PMMA – in the form of a polymeric/polymerizable tissue implant material. In the structural matrix provided by such a material, the contrast particles in Draenert are encapsulated in material that cures or hardens. The particles are thereby fixed or secured. Accordingly, there

is no concern or need to alter particle size in order to avoid particle migration in the Draenert matrix material. The particles are trapped therein. The asserted "optimization" of particle size offered by the teachings of Ersek has no applicability in the context of hard tissue implant applications.

Thus, Ersek offers no improvement or "optimization" of the Draenert disclosure. And Ersek's teachings would simply not be applied to the teachings of Draenert for the reason asserted by the examiner (*i.e.*, avoiding some deleterious effects of smaller particles). In actual practice, the lack of a need (or use) for acting on the asserted motivation is evident in the fact that contrast agent (*e.g.*, "conventional contrast agent") of a 1 μ to sub-micron size range is routinely used (and without concern) in hard tissue implant matrices such as disclosed in Draenert. For these reasons, it is asserted that one with skill in the art would not look to Ersek in modifying Draenert. As such, the proposed combination furthermore seeks to combine the teachings of non-analogous art.

Further in regard to the non-analogous nature of the art, it is noted that hard tissue implant matrices are required as a matter of structural support. In the case of vertebroplasty, the support provided offers a patient relief from, often, extreme pain and a possibility for improved mobility. In contrast, as shown in Figures 3 and 4 of Ersek, soft tissue augmentation is merely desirable to cosmetically treat depressed scar tissue or the like. Likewise, the matrix properties are not such to form a solid/structural mass. Taking such an approach would offer a discontinuous, and hence, incompatible pairing of physical properties with that of a soft tissue implantation site. To reiterate: especially in the case of vertebroplasty, hard tissue implant matrices must provide stiff structural support to the procedure's desired effect, while the opposite – *i.e.*, a non-rigid, malleable – consistency of the implant matrix is what is effective in cosmetic treatments in order that the implant go unnoticed.

Even if all this were not the case, the proposed modification of Draenert in view of Ersek is inappropriate because it will change the principle of operation of the base reference (Draenert). The proposed combination using Ersek's larger particles (up to 3mm), by far exceeds the applicable and/or acceptable size range of filler particles that can be used in Draenert. In fact, Draenert specifically states its maximum size for filler particles as "up to 250 μ m in size" (*i.e.*, 1/12th the size as might be employed in a Draenert/Ersek combination). Col. 3, line 39. The polymer particles in Draenert are themselves described as "no greater"/larger or only "up to 300 μ in size." Claim 1; Col. 3, line 40. Of course, such a particle could not cover or contain a radiographic filler particle any larger. Clearly, the particle size (be it filler or polymer particle size) is central to the operation of the Draenert invention. To simply use larger particles as in Ersek in modifying Draenert would quite obviously and unequivocally alter or destroy the reference's state utility in a manner prohibited by MPEP §2143.01. See also, *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Claims 37-39 and 46

In addition, no *prima facie* case has been made, particularly, with respect to claims 37-39 and 46 for reason of Ersek not teaching the use of two discreet sets of particles having sizes within differing ranges. Each of claims 37-39, but use of the phrase "further comprising" require not only the first set of particles called for in claim 36 from which they depend, but a second (smaller) set as well. Reference is made to the arguments above in regard to Ersek's failure to teach providing two discretely sized sets of particles.

Claim 35

Finally, it is noted that claim 35 requires that the mixture of the biocompatible matrix and said radiopaque particles of claim 33 form a hard tissue implant material. In other words, claim 35 requires that the matrix material be a hard tissue implant material. For the reasons that the teachings of Ersek do not apply as a motivation for combination with Draenert, Ersek

is further inapplicable to the invention of claim 35 as non-analogous art. Thus, Ersek is not applicable as a basis for rejecting claim 35. See, MPEP §2121.01(a).

It has already been explained above why the asserted reasons for applying Ersek in the hard tissue implant material setting (as put forth by the Examiner) are inapplicable. To restate the conclusion as pertinent to the question of analogous vs. nonanalogous art, one would not look to Ersek seeking solutions to problems actually experienced in the hard tissue implant material setting – at least not without applying hindsight reconstruction of Appellant's invention.

II. WHETHER A PRIMA FACIE CASE OF OBVIOUSNESS HAS BEEN ESTABLISHED BY VIRTUE OF PROPER COMBINATION OF ERSEK AND COOKE, OR – IF SO – WHETHER THE COMBINED TEACHINGS MEET THE LIMITATIONS OF CLAIMS 47-53

Claims 47-53

Claims 47- 53 are directed to an injectable composition comprising a hard tissue implant biocompatible matrix and radiopaque particles mixed in the biocompatible matrix, where the particles having a size between about 120 μ and about 2200 μ . Irrespective of the teachings of Cooke, modification of the same with Ersek is believed inappropriate. As argued above, Ersek is believed to represent art that is non-analogous to that for hard-tissue implants/hard tissue implant material. Simply, the problems voiced in Ersek as solved by that invention are not pertinent in the context of hard tissue implantation/implant material.

Arguments as to why are made above. Still further, reference is made to Appellant

Amendment filed December 19, 2002 amendment filed. In that paper, it was noted that:

In addition, it is asserted that the motivation expressed by the Examiner with respect to using the teaching of Ersek in connection with Cooke (avoiding the adverse – physiological – effects of smaller particles (col. 3, line 60 – col. 4 line 44; col. 6, lines 8-12) and taking into account variation from patient to patient (col. 5 line 64 = col. 6, line 2)) is not applicable to the context of hard tissue implants.⁴ In the context of hard tissue implantation, the use of very small

⁴ Applicant fails to see any reference in Ersek or elsewhere that using larger particles would aid in actual injection. The only discussion cited by the Examiner in Ersek has to do with the resulting presence of small particles (e.g., 60 μ particles). Unless the Examiner can support such a consideration without using Applicants specification as a guide in that regard, using larger particles to aid in injection should be withdrawn as an asserted motivation.

particles - even micron-sized particles (e.g., conventional contrast agent) - does not present a problem. In fact, none of claims 47-53 excludes the use of such particles in specifically calling for radiopaque particles between about 120 and about 2200 microns. The "open" nature of claim 47 (by virtue of the term comprising) allows for this possibility, as does the size range of particles noted in claim 53 which specifically calls for any size of particle up to 350 microns for contrast. For each of these reasons, the expressed motivation to avoid adverse physiological effects (macrophage engulfment as noted at col. 6, line 14 of the reference) is not pertinent.

Emphasis added. In short, there is no reason (not even those expressed by the Examiner) why one would look to Ersek to modify Cooke to reach Appellant's claimed invention.

Still further, in view of the comments above, it is once-again asserted that the motivation expressed by the Examiner in modifying Cooke in view of Ersek is inadequate to support a prima facie case of obviousness.

Claims 52 and 53

Finally, as noted in the cited text above, claims 52 and 53 specifically call for a composition including two distinct size ranges of particles. As previously asserted, Ersek presents no such teaching. Thus, these claims are believed allowable for such additional grounds besides those argued with respect to independent claim 47 from which they depend.

SUMMARY

Claims 40-44 are believed to be patentable over the §102 rejection(s) because Ersek does not disclose the use of particles having two different size ranges – much less, those claimed.

Claims 33-39 are believed to be patentable over the §103 rejections because the base reference (Draenert) is not properly modified by Ersek. The reasons expressed for the combination of references are simply not found in the reference as asserted by the Examiner and inapplicable as a motivation to modify Draenert. Also, the proposed modification of Draener would destroy its utility. Still further, because of the non-analogous nature of the art, one would not look to Ersek to modify Draenert. Likewise, application of Ersek to claim 35

which requires hard tissue implant material represents the application of non-analogous art. Finally, claims 37-39 and 46 offer additional grounds for patentability because Ersek fails to disclose the use of two sets of particles having sizes in particular (non-random) ranges.

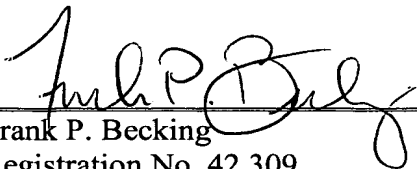
Claims 47-53 are believed to be patentable over the §103 rejections for reason of the inappropriate use/combination of non-analogous art and inadequate expression of a motivation for the proposed combination. Claims 52 and 53 offer additional grounds for allowably/patentability in view of Ersek's lack of teaching use of two particle size ranges within a composition.

RELIEF REQUESTED

Appellants respectfully request that the rejection of the claims under §§102(b) and 103(a) be reversed and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance. At minimum, remand of the application to the Examiner with instructions to put forth a prima facie case with respect to claims 33-39 and 46-53 is requested.

Respectfully submitted,

Date: 10/10/03


Frank P. Becking
Registration No. 42,309